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# Researchers Reverse Illness via Gene Therapy

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# Researchers Reverse Illness Via Gene Therapy

The first example of hereditary illness reversal by gene therapy was reported in the December 24 issue of *Nature* by researchers who described results of transferring a normal gene to bone marrow cells of diseased mice.

John Wolfe of the School of Veterinary Medicine at the University of Pennsylvania in Philadelphia, Edward Birkenmeier of The Jackson Laboratory in Bar Harbor, Maine, and their colleagues at Jackson and St. Louis University, have been researching Sly disease (MPS VII), a rare inherited disease found in humans, dogs, and mice. The disease is caused by an enzyme deficiency due to a defective gene and affects many organs, including the skeleton, heart, eye, liver, spleen, and brain.

Researchers were able to insert a normal copy of the gene that produces the enzyme into the defective stem cells of bone marrow in diseased mice, which resulted in unexpectedly striking reversal of the illness in the liver and spleen, despite low levels of enzyme activity in these organs.

Stem cells were used because they can permanently repopulate most tissues and the blood with cells that are derived from the bone marrow. While the disease was only corrected in a few tissues, the mice appeared to show clinical improvement, in that the mice were more active and looked healthier than age-matched untreated mice.

This research suggests new approaches for treatment of MPS and related diseases. "Eventually it may be possible to partially replace bone marrow in a patient with a small number of corrected stem cells, which may be sufficient to correct the genetic defects in the liver and spleen, without severe complications associated with total bone marrow removal," said Wolfe.

"It may also now be feasible to deliver therapeutically effective amounts of normal enzyme to patients by gene transfer to tissues such as muscle or the liver, in addition to the stem cells. Even though we've only been able to generate low levels of enzyme activity in the mice, the fact that the disease was reversed in



the liver and spleen may make it possible for significant and widespread improvement to occur if enough entry points are used for gene transfers. The cumulative effect of the low-level enzyme activity may prove to be an effective treatment."

In this form of gene therapy, a healthy copy of the defective gene is inserted into the DNA of cells from the patient. The treated cells are then returned to the patient, where it is hoped they will begin to perform their normal function in the body. One of the advantages of gene therapy in the treatment of Sly disease and related diseases is that eventually a patient will be treated by genetic engineering of his/her own tissue, thus eliminating the need for a matched donor, as is now standard procedure for traditional bone marrow transplantation. Researchers say new gene therapy methods eventually may produce greater clinical improvement than transplantation can.

Sly disease is one the group of inherited diseases (MPS disorders) caused by the deficiencies of enzymes required for degradation of complex sugar molecules. There may be little evidence of this at birth, but symptoms appear as more and more cells become damaged. Many patients have severe progressive disease, resulting in death at an early age. It is estimated that 1 in 25,000 births will result in some form of this disease.

The Medical Genetics group at the University of Pennsylvania's Veterinary School has a long history of investigat-

ing the genetics, biochemistry, pathology, and treatment of animals with genetic diseases. The Jackson Laboratory has been designated as a National Resource for the identification, characterization and distribution of mouse models of inherited human disease. Studies of these naturally-occurring counterparts of human genetic diseases have contributed to understanding both human and animal health.

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## Endowed Radiology Residency Established

Dr. Edward C. Preston of Southern Pines, North Carolina, a 1937 graduate of the Veterinary School and an active leader in civic affairs, has established a \$175,000 charitable remainder trust in honor of his 55th reunion. The trust, which provides Dr. Preston with lifetime income, will ultimately endow the Edward C. Preston Residency in Radiology. Dr. Preston's gift is one of largest gifts to the school from a living alumnus.

In Dr. Preston's words, "I have wanted to do something significant for the School for a long time. I feel privileged to be able to support radiology, an area of special interest to me, in gratitude for the education I received and, in particular, in recognition of the important role Drs. George Dick and Elias Booth, former faculty members, played in my life."